Kansas Drug Utilization Review Newsletter

Health Information Designs, LLC ***Summer 2016***

Welcome to the Summer 2016 edition of the "Kansas Drug Utilization Review Newsletter," published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites

KMAP Web Site
https://www.kmap-state-ks.us/

KDHE-DHCF Web Site
http://www.kdheks.gov/hcf/

KanCare Web Site
http://www.kancare.ks.gov/

Fee-For-Service (FFS) Helpful Numbers

Provider Customer Service (Provider Use Only)
1-800-933-6593

Beneficiary Customer Service
1-800-766-9012

KMAP PA Help Desk
1-800-285-4978

In This Issue:

Labeling Changes to Diabetic Medication Classes

Antidiabetic agents are among the most commonly used class for chronic disease states. There are nine classes of oral agents (alpha-glucosidase inhibitors, biguanides, bile acid sequestrants, dipeptidyl peptidase IV inhibitors, dopamine-2 agonists, meglitinides, sodium-glucose co-transporter 2 inhibitors, sulfonylureas, and thiazolidinediones) and three classes of injectable agents (amylin analogs, glucagon-like peptide 1 receptor agonists, and insulin) approved for the treatment of type 2 diabetes mellitus (T2DM). Kidney disease is highly prevalent in T2DM; renal impairment (eGFR < 60 mL/min/1.73 m2) occurs in approximately 20%-30% of diabetic patients.

On April 8, 2016, the U.S. Food and Drug Administration (FDA) revised warnings regarding the use of metformin in certain patients with reduced renal function. Previously, medication labeling and prescribing guidelines warned against the use of metformin in patients with certain serum creatinine (SCr) levels to reduce the risk of lactic acidosis in those with renal failure. This warning specifically targeted women with a SCr of ≥ 1.4 mg/dL and men with a SCr of ≥ 1.5 mg/dL. Metformin was FDA-approved in 1995 and has included a contraindication in these patient populations. After a review of numerous medical studies, the FDA concluded that metformin can be used safely in those with mild renal impairment and in some patients with moderate impairment. An additional recommendation from the FDA is to change the way a patient's renal function is evaluated; instead of a single laboratory parameter (serum creatinine), eGFR should be used to better estimate kidney function, taking into account additional parameters that are important, such as the patient's age, gender, race and/or weight.

The FDA is requiring manufacturers to revise labeling to recommend how and when kidney function is measured in patients receiving metformin. The revised labeling will include the following information:

1. Before starting metformin, obtain the patient's eGFR.
2. Metformin is contraindicated in patients with an eGFR below 30 mL/minute/1.73 m^2.
3. Starting metformin in patients with an eGFR between 30 - 45 mL/minute/1.73 m^2 is not recommended.
4. Obtain an eGFR at least annually in all patients taking metformin. In patients at increased risk for the development of renal impairment, such as the elderly, renal function should be assessed more frequently.

Labeling Changes to Diabetic Medication Classes cont.

5. In patients taking metformin whose eGFR later falls below 45 mL/minute/1.73 m^2, assess the benefits and risks of continuing treatment. Discontinue metformin if the patient's eGFR later falls below 30 mL/minute/1.73 m^2.
6. Discontinue metformin at the time of or before an iodinated contrast imaging procedure in patients with an eGFR between 30 and 60 mL/minute/1.73 m^2; in patients with a history of liver disease, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure; restart metformin if renal function is stable.

A list of FDA-approved metformin-containing medications are listed below:

Brand name	Active ingredient(s)
Actoplus Met	Metformin and pioglitazone
Actoplus Met XR	Metformin and pioglitazone, extended release
Avandamet	Metformin and rosiglitazone
Fortamet	Metformin extended release
Glucophage	Metformin
Glucophage XR	Metformin extended release
Glucovance	Metformin and glyburide
Glumetza	Metformin extended release
Invokamet	Metformin and canagliflozin
Janumet	Metformin and sitagliptin
Janumet XR	Metformin and sitagliptin, extended release
Jentadueto	Metformin and linagliptin
Kazano	Metformin and alogliptin
Kombiglyze XR	Metformin and saxagliptin, extended release
Prandimet	Metformin and repaglinide
Riomet	Metformin
Synjardy	Metformin and empagliflozin
Xigduo XR	Metformin and dapagliflozin, extended release

While metformin is in the process of having restrictions for renal impairment lifted, the FDA is strengthening its warnings for many agents in the class of drugs called sodium-glucose cotransporter-2 (SGLT2) inhibitors. Active ingredients of canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR) have had recent reports of acute kidney injury. Risk factors that predispose patients to acute kidney injury include decreased blood volume; chronic kidney insufficiency; congestive heart failure; and taking other medications such as diuretics, blood pressure medicines called angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs (NSAIDs). Canagliflozin has had 101 confirmable cases of acute kidney injury, some requiring hospitalization and dialysis, from its approval in March 2013 to October 2015; this only includes reported cases. The highest risk, and occurring in half of the cases, is seen within one month of starting the medication.

Labeling Changes to Diabetic Medication Classes cont.

Healthcare providers are encouraged to report adverse events involving canagliflozin, dapagliflozin, or other drugs to the FDA MedWatch program by completing and submitting the report online. Download the form, or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

Additionally, the FDA has published a safety announcement for canagliflozin due to the interim safety results from an ongoing clinical trial (Canagliflozin Cardiovascular Assessment Study [CANVAS]) that found an increased risk of leg and foot amputations, mostly affecting the toes. The amputations occurred about twice as often in patients treated with canagliflozin compared to patients treated with placebo. An interim analysis showed that over a year's time, the risks of amputation for patients in the trial were equivalent to the following: 7 out of every 1,000 patients treated with 100 mg daily of canagliflozin; 5 out of every 1,000 patients treated with 300 mg daily of canagliflozin; 3 out of every 1,000 patients treated with placebo. Patients in the CANVAS trial have been followed for an average of 4.5 years to date.

The trial's independent data monitoring committee (IDMC) has recommended, based on an overall assessment, that the CANVAS trial continue. The IDMC has also reported that a second similar trial evaluating canagliflozin, the CANVAS-R trial, has not shown the same risk of increased leg and foot amputations to date. Patients in the CANVAS-R trial have been followed for an average of nine months.

There are additional agents that have warning and precautions in the use of those with kidney impairment, and their limitations have not been lifted (e.g., glyburide, DPP-IV inhibitors, GLP-1 agonists).

References:

1. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Farrannini E, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2012; 35: 1364-79.
2. U.S. Food and Drug Administration. Canagliflozin (Invokana, Invokamet): drug safety communication – clinical trial results find increased risk of leg and foot amputations. May 18, 2016. Available at http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm501565.htm.
3. U.S. Food and Drug Administration. Canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR): drug safety communication – strengthened kidney warnings. June 14, 2016. Available at http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm506554.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery.
4. U.S. Food and Drug Administration. FDA drug safety communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function. April 8, 2016. Available at http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm.

Generic Medications

Recently Approved Generic Drugs:

June 2016	July 2016	August 2016
Dofetalide (Tkiosyn) Fosaprepitant (Emend) Dasatinib (Sprycel) Fenofibrate (Fenoglide) Hydrocodone ER (Exalgo)	Nilutamide (Nilandron) Rosuvastatin (Crestor)	Zolpidem Sublingual (Edluar) Oseltamivir (Tamiflu) Doxylamine-pyridoxine (Diclegis)

Upcoming Generic Drugs:

Generic Name	Brand Name	Anticipated Launch
Estradiol	Vagifem	October 1, 2016
Amlodipine-Olmesartan	Azor	October 25, 2016
Olmesartan; Olmesartan-HCTZ	Benicar and Benicar HCT	October 25, 2016
Quetiapine	Seroquel XR	November 1, 2016
Bosentan	Tracleer	November 1, 2016
Abacavir-lamivudine	Epzicom	November 18, 2016
Oseltamivir	Tamiflu	December 1, 2016
Drospirenone-ethinyl estradiol-levomefolate	Beyaz	December 1, 2016
Drospirenone-ethinyl estradiol-levomefolate	Safyral	December 1, 2016
Ezetimibt	Zetia	December 12, 2016
Albuterol	Proair HFA	December 19, 2016
Eletriptan	Relpax	December 26, 2016

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